

REMARKS

Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejections in view of the foregoing amendments and following remarks. Claim 6 has been amended to include the moiety "R" in the structural of formula II (The "R" was inadvertently omitted in the last response).

Claims 6, 17, 18, 21 and 28-31 stand rejected under 35 U.S.C. 102(b) as being anticipated by Oberdorf et al. (USP 6,114,342). Applicants respectfully submit that Oberdorf does not teach each and every element of the present claims for the following reasons.

Present claim 6 requires the use of an indium or iron based catalyst that can be in the form of the metal or halides, oxides or triflates thereof. Oberdorf does not disclose the use of an indium or iron based catalyst. The only teaching of catalytic reagents in Oberdorf is at column 3, lines 17-31, which discloses that it may be advantageous to use 18-crown-6 or 15-crown-5 as a catalyst. This section of Oberdorf also teaches that, if a biphasic system is used, phase transfer catalysts such as ammonium halides or ammonium tetrafluoroborates can be used.

Moreover, the cited passage of Oberdorf in the outstanding Office Action (col. 3, lines 60-67) discloses halides. However, this passage does not teach or suggest a catalyst that contains iron or indium. To carry out the ether cleavage, Oberdorf teaches a molar excess of boron trichloride or hydrogen bromide, wherein neither of these compounds is used in a catalytic manner. Once again, Oberdorf does not teach or suggest the use of either indium or iron, or halides, oxides or triflates thereof, as catalysts.

Further with respect to Oberdorf, the examiner has stated at page 8, 2nd paragraph of the Office Action, that there is a teaching of equivalence among hydrogen chloride and hydrogen bromide. Applicants respectfully submit that this interpretation is not correct. To support this position, Applicants have included a German language excerpt of Morrison and Boyd "Lehrbuch der Organischen Chemie." On page 611 of the German text, it is described that the reactivity of HX for the cleavage of ethers is not equivalent. Hydrogen iodine is the most reactive and hydrogen chloride is the least reactive compound in this context. Accordingly, it is known in textbooks on organic chemistry that ether cleaving reactions can be done with HI or HBr if the corresponding iodo- or bromo- compounds are desired. If, on the other hand, a chloro- compound is desired, it is known in the art to use Lewis-acids such as BCl₃ – which is consistent with the Oberdorf teaching (cf. column 5, lines 45 to 50).

Therefore, Applicants respectfully submit that since Oberdorf does not teach or suggest the use of an indium or iron based catalyst, Oberdorf cannot anticipate the present claims. Furthermore, Applicants submit that the teaching of HCl in the present claims is not the equivalent of using HBr as described in Oberdorf.

Claims 6 and 8-31 stand rejected under 35 U.S.C. 103(a) as being obvious over Oberdorf et al (USP 6,114,342) in view of Jempty et al (J. Org. Chem. 1981, Vol. 46, 4545-4546) and Moody et al. (Synlett. 1999, No. 10, 1575-1576). Applicants respectfully submit that the combination of these documents cannot render obvious the present claims.

As argued above, Applicants submit that Oberdorf does not disclose each and every element of the claims.

Jempty discloses using iron chloride supported on silica gel as a means for ether cleavage. The disclosure of Jempty, and the section on page 7 of the outstanding Office Action relied upon by the Examiner, states that the silica supported iron chloride is used in a 1.1 molar ratio versus the starting materials, which leads the skilled artisan away from using it in only catalytic amounts, as required by the present claims. Applicants submit that this ratio would be recognized by one of ordinary skill in the art as a ratio *not* indicative of catalytic reagents.

Therefore, one of skill in the art who combined the disclosures of Oberdorf and Jempty would not arrive at either indium or iron catalysts as required by present claim 6. Applicants submit that the disclosure of Jempty does not cure the deficiencies of Oberdorf because a combination of the two disclosures would lead to the use of chlorides in stoichiometric amounts. Neither document teaches or suggests the use of catalytic amounts.

Moody teaches the use of indium metal as a reducing agent in the cleavage of benzyl ethers. Moody is silent with respect to any mention of the indium being used in a catalytic manner.

A skilled artisan reading this reference is led away from the present claims for the following reasons. Moody describes the reaction as follows, "*On treatment with indium metal, the nitro group is reduced, and the benzylic C-O bond is cleaved.,.*" Applicants respectfully submit that disclosure means that the reaction depends on the nitro group reduction to take place before the ether cleaving event takes place. However, the present claims do not require the ether cleaving event to be dependent first upon nitro group reduction because a nitro group is not included in the starting compounds according to the

present claims. Thus, the skilled artisan would not believe that the reaction described in that reference would be applicable to ether cleaving the compounds of the present claims.

Furthermore, Moody discloses that "...benzyl ethers remained intact, demonstrating the selectivity of the reaction." Since the reactions of the present claims require a benzyl ether to be cleaved, the skilled artisan would be lead to think that the reaction described in this reference would not be applicable to ether cleaving the compounds of the present claims. Moreover, Moody does not disclose cleavage of benzyl ethers, but rather the cleavage of the specific benzylic C-O bond of the 4-nitrobenzyl moiety. Therefore, the disclosure of Moody does not cure the deficiencies of Oberdorf or Jempty, either alone or in combination with each other.

The present claims require the use of catalytic amounts of an indium or iron metal, or halides, oxides or triflates thereof. Applicants submit that one of skill in the art who combined the disclosures of Oberdorf, Jempty and Moody would arrive at a system that employed indium or iron halides in a non-catalytic manner. Applicants submit that the present claims are not rendered obvious by the combination of Oberdorf, Jempty and Moody. For these reasons, Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejection. Early and favorable action is awaited.

Respectfully submitted,

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Morrison/Boyd

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Chemie**

3. Auflage



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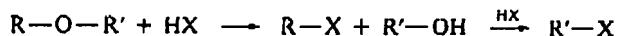
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12.7 Reaktionen der Ether. Spaltung durch Säuren 611

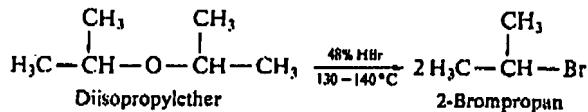
12.7 Reaktionen der Ether. Spaltung durch Säuren

Ether sind relativ reaktionsträge Verbindungen. Die Etherbindung ist gegenüber Basen, Oxidationsmitteln und Reduktionsmitteln ziemlich stabil. Wenn man nur diese Bindung betrachtet, gehen Ether lediglich eine Art von Reaktion ein, die Spaltung durch Säuren:

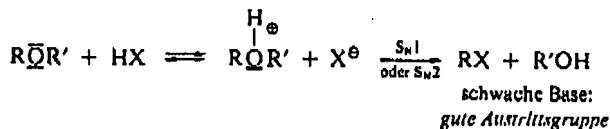


Reaktivität von HX: HI > HBr > HCl

Die Spaltung erfolgt erst unter äußerst drastischen Reaktionsbedingungen. Konzentrierte Säuren (gewöhnlich HI oder HBr) müssen bei hoher Temperatur auf den Ether einwirken. Aus einem Dialkylether entstehen zunächst ein Alkylhalogenid und ein Alkohol. Letzterer kann zu einem zweiten Molekül Alkylhalogenid weiterreagieren. Zum Beispiel:



Bei der Spaltung wird der protonierte Ether von dem Halogen-Anion nucleophil angegriffen, wobei das schwach basische Alkoholmolekül verdrängt wird:



Eine solche Reaktion erfolgt wesentlich rascher als die Verdrängung des stark basischen Alkoholat-Ions aus dem neutralen Ether.



Die Reaktion eines protonierten Ethers mit einem Halogenid-Ion kann wie die entsprechende Reaktion eines protonierten Alkohols entweder nach einem S_N1 - oder nach einem S_N2 -Mechanismus erfolgen, je nach den Reaktionsbedingungen und der Struktur des Ethers. Erwartungsgemäß neigt eine primäre Alkylgruppe zu einer S_N2 -Reaktion, eine tertiäre Alkylgruppe dagegen zu einer S_N1 -Reaktion.

S_N1

